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L9 ANSWER 1 OF 7 HCPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2004:397248 HCPLUS  
TITLE: Reduced calcification of bioprostheses, cross-linked  
via an improved carbodiimide based method  
AUTHOR(S): Everaerts, Frank; Torrianni, Mark;  
van Luyn, Marja; van Wachem, Pauline; Feijen, Jan;  
Hendriks, Mark  
CORPORATE SOURCE: Biomaterials S&T, Medtronic Bakken Research Center,  
Maastricht, 6229 GW, Neth.  
SOURCE: Biomaterials (2004), 25(24), 5523-5530  
CODEN: BIMADU; ISSN: 0142-9612  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Glutaraldehyde fixation of bioprosthetic tissue has been used successfully for almost 40 yr. However, it is generally recognized that glutaraldehyde fixation of bioprostheses is associated with the occurrence of calcification. Accordingly, many efforts have been undertaken to develop techniques for the fixation of bioprostheses, which will not lead to calcification. Here we describe a new improved carbodiimide based **crosslinking** method. Rather than **crosslinking** the tissue through its free primary amine groups, these groups were first blocked with butanal and the tissue was then cross-linked by means of carbodiimide activation of tissue carboxylic acid groups followed by a reaction with a poly(propylene glycol)bis 2-(aminopropyl) ether, (Jeffamine). It was demonstrated that cross-linked porcine leaflets had a calcification of less than 1 mg/g tissue after 8 wk sub-dermal implantation in rats. Furthermore, aortic wall calcification was reduced to 50 mg/g, compared to standard glutaraldehyde fixed tissue, which showed 120 mg/g tissue calcification in the 8 wk calcification model used.

CC 63-7 (Pharmaceuticals)

ST carbodiimide heart valve bioprosthetic

IT Calcification

**Crosslinking**

(reduced calcification of bioprostheses, cross-linked via an improved carbodiimide based method)

IT Heart

(valve, bioprosthetic; reduced calcification of bioprostheses, cross-linked via an improved carbodiimide based method)

IT 7440-70-2, Calcium 7723-14-0, Phosphorus

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(reduced calcification of bioprostheses, cross-linked via an improved carbodiimide based method)

IT 123-72-8, Butanal

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); PROC (Process)

(reduced calcification of bioprostheses, cross-linked via an improved carbodiimide based method)

IT 9046-10-0, Jeffamine 400

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(reduced calcification of bioprostheses, cross-linked via an improved carbodiimide based method)

IT 1892-57-5, 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide 6066-82-6, N-Hydroxysuccinimide

RL: RCT (Reactant); RACT (Reactant or reagent)

(reduced calcification of bioprostheses, cross-linked via an improved carbodiimide based method)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2003:950040 HCAPLUS  
 DOCUMENT NUMBER: 140:19764  
 TITLE: Methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells  
 INVENTOR(S): McKay, William F.; Boden, Scott D.; Yoon, Sangwook T.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 81 pp., Cont.-in-part of U.S. Ser. No. 292,951.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003225021	A1	20031204	US 2003-382844	20030307
US 2003180266	A1	20030925	US 2002-292951	20021113
PRIORITY APPLN. INFO.:			US 2001-331321P	P 20011114
			US 2002-292951	A2 20021113
			US 1988-124238	A 19880729
			US 2000-959578	A 20000428

AB A method of inducing the expression of one or more bone morphogenetic proteins and/or transforming growth factor- $\beta$  proteins in a cell is described. The method includes transfecting a cell with an isolated nucleic acid comprising a nucleotide sequence encoding a LIM mineralization protein operably linked to a promoter. The one or more bone morphogenetic proteins can be BMP-2, BMP-4, BMP-6, BMP-7 or combinations thereof. The transforming growth factor- $\beta$  protein can be transforming growth factor- $\beta$ 1 protein (TGF- $\beta$ 1). Transfection may be accomplished ex vivo or in vivo by direct injection of virus or naked DNA, or by a nonviral vector such as a plasmid. The method can be used to induce bone formation in osseous cells or to stimulate proteoglycan and/or collagen production in cells capable of producing proteoglycan and/or collagen (e.g., intervertebral disk cells).

IC ICM A61K048-00

ICS C12N005-08; C12N015-861; C12N015-867

NCL 514044000; 424093200; 435456000; 435366000

CC 63-1 (Pharmaceuticals)

Section cross-reference(s): 3, 6, 14

ST bone morphogenetic protein transforming growth factor gene therapy; BMP TGF gene bone formation intervertebral disk disease; oligonucleotide transformation cell implant bone disease

IT Bone morphogenetic proteins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (2; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Bone morphogenetic proteins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

- (4; methods of inducing the expression of **bone morphogenetic proteins (BMPs)** and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)
- IT **Bone morphogenetic proteins**  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(6; methods of inducing the expression of **bone morphogenetic proteins (BMPs)** and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)
- IT **Bone morphogenetic proteins**  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(7; methods of inducing the expression of **bone morphogenetic proteins (BMPs)** and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)
- IT **Adenoviridae**  
(AdLMP-1; methods of inducing the expression of **bone morphogenetic proteins (BMPs)** and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)
- IT **Gene, animal**  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BMP-2; methods of inducing the expression of **bone morphogenetic proteins (BMPs)** and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)
- IT **Gene, animal**  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BMP-4; methods of inducing the expression of **bone morphogenetic proteins (BMPs)** and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)
- IT **Gene, animal**  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BMP-6; methods of inducing the expression of **bone morphogenetic proteins (BMPs)** and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)
- IT **Gene, animal**  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BMP-7; methods of inducing the expression of **bone morphogenetic proteins (BMPs)** and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)
- IT **Proteins**  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(HLMP-1; methods of inducing the expression of **bone morphogenetic proteins (BMPs)** and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)
- IT **Proteins**  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(HLMP-1s; methods of inducing the expression of **bone morphogenetic proteins (BMPs)** and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)
- IT **Proteins**  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(HLMP-2; methods of inducing the expression of **bone morphogenetic proteins (BMPs)** and transforming growth factor-beta

proteins (TGF- $\beta$ s) in cells)

IT Proteins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(HLMP-3; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Proteins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(LIM domain-containing; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Proteins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(LMP-1; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Proteins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(RLMP; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Gene, animal  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(TGF- $\beta$ 1; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Cell  
(annulus fibrosus; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Spinal column, disease  
(intervertebral disk hernia; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Spinal column  
(intervertebral disk; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Stem cell  
(mesenchymal; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Adenoviral vectors  
Bone formation  
Gene therapy  
Genetic vectors  
Hematopoietic precursor cell  
Mammalia  
Mesenchyme  
Molecular cloning  
Nucleic acid hybridization  
Ore genesis  
Plasmid vectors  
Retroviral vectors  
Retroviridae

Transformation, genetic  
 Transplant and Transplantation  
 Viral vectors  
 Virus  
 (methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Oligonucleotides  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Bone morphogenetic proteins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Nucleic acids  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Promoter (genetic element)  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Cytomegalovirus  
 (promoter; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Cell nucleus  
 (pulposus; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Animal cell  
 (somatic; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT Transforming growth factors  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 ( $\beta$ -; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT 630143-01-0 630143-02-1  
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (oligonucleotide; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT 630150-76-4 630150-77-5 630150-78-6 630150-79-7 630150-80-0  
 630150-81-1 630150-82-2 630150-83-3 630150-85-5 630150-86-6  
 630150-87-7 630150-88-8 630150-89-9 630150-90-2 630150-91-3  
 630150-92-4 630150-93-5 630150-94-6 630150-95-7 630150-96-8  
 630150-97-9 630150-98-0 630150-99-1 630151-00-7 630151-01-8

630151-02-9 630151-03-0 630151-04-1 630151-06-3 630151-07-4  
 630151-08-5 630151-10-9 630151-12-1 630151-13-2

RL: PRP (Properties)

(unclaimed nucleotide sequence; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT 630150-75-3 630150-84-4 630151-05-2 630151-09-6 630151-11-0

RL: PRP (Properties)

(unclaimed protein sequence; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

IT 630151-14-3 630151-15-4 630151-16-5 630151-17-6 630151-18-7

630151-19-8 630151-20-1 630151-21-2 630151-22-3

RL: PRP (Properties)

(unclaimed sequence; methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF- $\beta$ s) in cells)

L9 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:397004 HCAPLUS

DOCUMENT NUMBER: 138:397329

TITLE: cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury

INVENTOR(S): McKay, William F.; Boden, Scott D.; Yoon, Sangwook T.

PATENT ASSIGNEE(S): Medtronic Sofamor Danek, USA

SOURCE: PCT Int. Appl., 94 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003042368	A2	20030522	WO 2002-US36465	20021114
WO 2003042368	A3	20031016		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, 'AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003180266	A1	20030925	US 2002-292951	20021113
PRIORITY APPLN. INFO.:			US 2001-331321P	P 20011114
			US 2002-292951	A 20021113
			US 1988-124238	A 19880729
			US 2000-959578	A 20000428

AB Methods of expressing LIM mineralization protein in non-osseous mammalian cells, such as stem cells or intervertebral disk cells (e.g., cells of the annulus fibrosus, or cells of the nucleus pulposus) are described. The methods involve transfecting the cells with an isolated nucleic acid comprising a nucleotide sequence encoding a LIM mineralization protein operably linked to a promoter. Transfection may be accomplished ex vivo

or in vivo by direct injection of virus or naked DNA, or by a nonviral vector such as a plasmid. Expression of the LIM mineralization protein can stimulate proteoglycan and/or collagen production in cells capable of producing proteoglycan and/or collagen. Methods for treating disk disease associated with trauma or disk degeneration are also described.

- IC ICM C12N  
 CC 3-3 (Biochemical Genetics)  
 Section cross-reference(s): 1, 6, 13  
 ST cDNA LIM mineralization protein human rat sequence; disk degeneration injury therapy LMP protein splicing isoform  
 IT **Bone morphogenetic proteins**  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (2, LMP protein in stimulating synthesis of; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)  
 IT Adenoviral vectors  
 (AdHLMP-1, LIM mineralization protein cDNA cloning in; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)  
 IT Protein motifs  
 (LIM domain, in LMP proteins; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)  
 IT Plasmid vectors  
 Retroviral vectors  
 Viral vectors  
 (LIM mineralization protein cDNA cloning in; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)  
 IT Proteoglycans, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (LIM mineralization protein in stimulating synthesis of; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)  
 IT mRNA  
 RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)  
 (LIM mineralization protein; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)  
 IT cDNA  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (LIM mineralization protein; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)  
 IT Proteins  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (LMP (LIM mineralization protein), isoforms 1,2 and 3, of rat and human; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)  
 IT **Bone morphogenetic proteins**  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (LMP protein in inducing synthesis of; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)  
 IT Osteocalcins  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)

- (LMP protein in stimulating secretion of; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)
- IT **Collagens, biological studies**  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (LMP protein in stimulating synthesis of, as carrier for LMP protein implant in vertebral disk; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)
- IT **Aggrecans**  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (LMP protein in stimulating synthesis of; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)
- IT **Bone formation**  
 (LMP protein in; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)
- IT **RNA splicing**  
 (LMP protein mRNA; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)
- IT **Body, anatomical**  
 (back, disease, pain, lower; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)
- IT **Pain**  
 (back, lower; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)
- IT **Animal cell**  
 Gene therapy  
 Human  
 Mammalia  
 Nucleic acid hybridization  
 Rattus  
 (cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)
- IT **Promoter (genetic element)**  
 RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (cytomegalovirus, for LMP proteins synthesis; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)
- IT **Bone, disease**  
 (degenerative disk disease, spine stenosis; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)
- IT **Probes (nucleic acid)**  
 RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (for LMP protein cDNA; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)
- IT **Primers (nucleic acid)**  
 RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (for LMP protein cDNA; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk

injury)

IT cDNA sequences  
(for LMP proteins of human and rat; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Drug delivery systems  
(implants, LMP protein in; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Drug delivery systems  
(injections, LMP protein in; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Spinal column, disease  
(intervertebral disk hernia; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Spinal column  
(intervertebral disk; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Spinal cord  
(lumbar, fusion, LMP protein in gene therapy in; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Bone formation  
(mineralization, LMP protein in; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Molecular cloning  
(of LIM mineralization proteins; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Protein sequences  
(of LMP proteins of human and rat; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Cell differentiation  
(osteoblast, LMP protein in; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Stem cell  
(pluripotent, LIM mineralization protein mRNA in; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Cytomegalovirus  
(promoter for LMP proteins synthesis; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Mutation  
(splice site, LMP protein; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Glycosaminoglycans, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(sulfated, LMP protein in inducing synthesis of; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Polymers, biological studies  
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological

study); USES (Uses)  
 (synthetic, as carrier for LMP protein containing cell used in intervertebral disk implant; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT Spinal column  
 (vertebra, annulus fibrosus, nucleus pulposus, LIM mineralization protein mRNA in; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT 530167-58-9 530167-59-0 530167-62-5 530167-64-7  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (amino acid sequence; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT 256606-43-6, GenBank AC023788  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT 530167-57-8 530167-60-3 530167-61-4 530167-63-6  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (nucleotide sequence; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT 530167-30-7 530167-31-8  
 RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (primer sequence; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT 530170-01-5, 3: PN: WO03042368 SEQID: 3 unclaimed DNA 530170-02-6  
 530170-03-7 530170-04-8, 6: PN: WO03042368 SEQID: 6 unclaimed DNA  
 530170-05-9, 7: PN: WO03042368 SEQID: 7 unclaimed DNA 530170-06-0, 8:  
 PN: WO03042368 SEQID: 8 unclaimed DNA 530170-07-1 530170-08-2  
 530170-09-3 530170-10-6 530170-11-7 530170-12-8 530170-13-9  
 530170-14-0 530170-15-1 530170-16-2 530170-17-3 530170-18-4  
 530170-19-5 530170-20-8 530170-21-9 530170-22-0 530170-23-1  
 530170-24-2 530170-25-3 530170-26-4 530170-28-6 530170-29-7  
 530170-30-0 530170-31-1 530170-33-3 530170-34-4 530170-35-5  
 530170-36-6 530170-37-7 530170-38-8 530170-39-9 530170-40-2  
 RL: PRP (Properties)  
 (unclaimed nucleotide sequence; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT 530170-27-5  
 RL: PRP (Properties)  
 (unclaimed protein sequence; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

IT 530158-96-4  
 RL: PRP (Properties)  
 (unclaimed sequence; cDNAs encoding rat and human LIM mineralization proteins and their use in treatment of disk degeneration and disk injury)

L9 ANSWER 4 OF 7 HCPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:181215 HCAPLUS  
 DOCUMENT NUMBER: 137:358009  
 TITLE: Optimization of diamine bridges in glutaraldehyde treated bioprosthetic aortic wall tissue  
 AUTHOR(S): Human, Paul; Bezuidenhout, Deon; Torrianni, Mark; Hendriks, Marc; Zilla, Peter  
 CORPORATE SOURCE: Cape Heart Centre, Department of Cardiothoracic Surgery, University of Cape Town, Cape Town, S. Afr.  
 SOURCE: Biomaterials (2002), 23(10), 2099-2103  
 CODEN: BIMADU; ISSN: 0142-9612  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Objective: Bioprosthetic calcification can be significantly mitigated by both increased concns. of glutaraldehyde (GA) and the introduction of diamine (DA) bridges. The purpose of the present study was to evaluate whether an optimal effect of DA-enhanced fixation can be achieved by titration of dialdehyde and diamine concns. Methods: Porcine aortic roots were fixed at 0.05% GA (under-fixation) or 0.2% GA and 0.7% GA (com. fixation). An interim step of DA treatment (L-Lysine; 0, 25, 50 or 100 mm; 37°C; 2 days) was followed by completion of the GA fixation (37°C; 5 days). Aortic wall coupons (12 mm) were punched out and implanted s.c. into seven-week old Long-Evans rats for 60 days. Calcium content was assessed by atomic absorption spectroscopy and histol. Results: Increasing the L-Lysine concns. beyond 25 mm was essential to achieve the anti-calcific effect of DA-enhanced fixation. This effect was proportional to the GA concns. applied. Compared to non-enhanced GA fixation (0 mm DA), calcification increased by 17.4% ( $p=0.2114$ ) in 0.05% fixed tissue but decreased by 32.0% ( $p<0.0001$ ) and 45.1% ( $p<0.0002$ ) in 0.2% and 0.7% GA, resp., when the DA concentration was 100 mm. Histol. the extent, but not the pattern of calcification, was affected. Conclusion: The calcium mitigating effect of diamine-treatment as an interim step of glutaraldehyde fixation is proportional to the GA concentration applied.

Within  
 com. 0.7% GA fixation 100 mm DA has the potential to practically halve aortic wall calcification.

CC 63-7 (Pharmaceuticals)

ST aorta glutaraldehyde crosslinking calcification

IT Artery  
 (aorta; optimization of diamine bridges in glutaraldehyde treated bioprosthetic aortic wall tissue)

IT Prosthetic materials and Prosthetics  
 (bioprosthetics; optimization of diamine bridges in glutaraldehyde treated bioprosthetic aortic wall tissue)

IT Amines, formation (nonpreparative)  
 RL: FMU (Formation, unclassified); FORM (Formation, nonpreparative)  
 (diamines; optimization of diamine bridges in glutaraldehyde treated bioprosthetic aortic wall tissue)

IT Calcification  
 Crosslinking  
 (optimization of diamine bridges in glutaraldehyde treated bioprosthetic aortic wall tissue)

IT Heart  
 (valve, bioprosthetic; optimization of diamine bridges in glutaraldehyde treated bioprosthetic aortic wall tissue)

IT 56-87-1, L-Lysine, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (optimization of diamine bridges in glutaraldehyde treated bioprosthetic aortic wall tissue)

IT 111-30-8, Glutaraldehyde

RL: MOA (Modifier or additive use); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)

(optimization of diamine bridges in glutaraldehyde treated bioprosthetic aortic wall tissue)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:553459 HCAPLUS

DOCUMENT NUMBER: 133:155511

TITLE: Highly-mineralized osteogenic sponge compositions, and uses thereof

INVENTOR(S): McKay, William F.

PATENT ASSIGNEE(S): SDGI Holdings, Inc., USA

SOURCE: PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000045871	A1	20000810	WO 2000-US3043	20000204
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1150726	A1	20011107	EP 2000-905989	20000204
EP 1150726	B1	20031105		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002536077	T2	20021029	JP 2000-596990	20000204
AT 253385	E	20031115	AT 2000-905989	20000204
AU 772682	B2	20040506	AU 2000-27568	20000204
ES 2209820	T3	20040701	ES 2000-905989	20000204
PRIORITY APPLN. INFO.:			US 1999-118615P	P 19990204
			WO 2000-US3043	W 20000204

AB Osteogenic sponge compns. having enhanced osteoinductive properties for use in **bone** repair are described. The compns. include a quickly resorbable porous carrier, a more slowly resorbed mineral scaffold and an osteogenic factor, preferably a **bone** morphogenetic protein. The compns. enable increased osteoinductive activity while retaining a reliable scaffold for the formation of new **bone** at an implant site. Methods for therapeutic use of the compns. are also described.

IC ICM A61L027-22  
ICS A61L027-56; A61L027-46; A61K038-18

CC 63-7 (Pharmaceuticals)

Section cross-reference(s): 2

ST osteogenic sponge morphogenetic protein **bone** implant

IT **Bone** morphogenetic proteins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(2; highly-mineralized osteogenic sponge compns. for repair of bone)

IT **Bone morphogenetic proteins**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(7; highly-mineralized osteogenic sponge compns. for repair of bone)

IT **Proteins, specific or class**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(LMP (LIM-mineralization proteins); highly-mineralized osteogenic sponge compns. for repair of bone)

IT **Ceramics**  
 (biocompatible; highly-mineralized osteogenic sponge compns. for repair of bone)

IT **Bone formation**

Osteoblast

Osteoclast

Particle size distribution

(highly-mineralized osteogenic sponge compns. for repair of bone)

IT **Bone morphogenetic proteins**

Collagens, biological studies

Platelet-derived growth factors

Steroids, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(highly-mineralized osteogenic sponge compns. for repair of bone)

IT **Bone**

(implant; highly-mineralized osteogenic sponge compns. for repair of bone)

IT **Porosity**

(microporosity; highly-mineralized osteogenic sponge compns. for repair of bone)

IT **Bone marrow**

(osteogenic enhancing factor of; highly-mineralized osteogenic sponge compns. for repair of bone)

IT **Growth factors, animal**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(osteogenins; highly-mineralized osteogenic sponge compns. for repair of bone)

IT **Bone**

(particles of; highly-mineralized osteogenic sponge compns. for repair of bone)

IT **Surgery**

(spinal fusion; highly-mineralized osteogenic sponge compns. for repair of bone)

IT **Medical goods**

(sponges, osteogenic; highly-mineralized osteogenic sponge compns. for repair of bone)

IT **Spinal column**

(vertebra, fusion of; highly-mineralized osteogenic sponge compns. for repair of bone)

- IT Transforming growth factors  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (β-; highly-mineralized osteogenic sponge compns. for repair of bone)
- IT Microglobulins  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (β-microglobulins; highly-mineralized osteogenic sponge compns. for repair of bone)
- IT 10103-46-5, Calcium phosphate  
 RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (biocompatible ceramics; highly-mineralized osteogenic sponge compns. for repair of bone)
- IT 61912-98-9, Insulin like growth factor 62031-54-3, Fgf  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (highly-mineralized osteogenic sponge compns. for repair of bone)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:139773 HCAPLUS

DOCUMENT NUMBER: 130:200953

TITLE: A method of **crosslinking** collagen-based material and bioprosthetic devices produced therefrom  
 INVENTOR(S): Hendriks, Marc; Verhoeven, Michel; Cahalan, Patrick T.; Torrianni, Mark W.; Fouache, Benedicte; Cahalan, Linda

PATENT ASSIGNEE(S): Medtronic, Inc., USA

SOURCE: Eur. Pat. Appl., 26 pp.  
 CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 897942	A1	19990224	EP 1998-306595	19980818
EP 897942	B1	20040310		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6166184	A	20001226	US 1997-912778	19970818

PRIORITY APPLN. INFO.: US 1997-912778 A 19970818

AB Methods of crosslinking collagen-based material having collagen amine groups and collagen carboxyl groups are provided. The methods comprise blocking at least a portion of the collagen amine groups with a blocking agent to form blocked amine groups; contacting the collagen-based

material having the blocked amine groups with a polyfunctional spacer; and activating at least a portion of the collagen carboxyl groups after blocking at least a portion of the collagen amine groups, wherein the polyfunctional spacer crosslinks the collagen-based material and wherein said contacting step may be effected before or after said activating step. Bioprosthetic devices made from these crosslinked collagen-based materials are also provided. Crosslinking involving the JEFFAMINE spacers shows the fastest rehydration, whereas glutaraldehyde crosslinking tends to be a bit slower. The highly hydrophilic crosslinked collagen-derived materials promote infiltration and diffusion of tissue fluid through the material matrix, providing supply of oxygen, nutritive substances, electrolytes and drainage of metabolites. Also, ingrowth of capillary blood vessels and cells is promoted, and consequently the healing response is improved. In addition, hydrophilicity improves the blood compatibility of the material. Collagen samples crosslinked according to the method of the invention involving the Jeffamine D230 spacer had a cell growth inhibition of 25%, while cells with a deviant morphol. were not observed

- IC ICM C08H001-06  
 ICS A61L027-00  
 CC 63-7 (Pharmaceuticals)  
 Section cross-reference(s): 45  
 ST crosslinking collagen bioprosthetic device manuf  
 IT Acylation  
     (agents; crosslinking collagen-based material for  
     bioprosthetic devices manufature)  
 IT Heart  
     (aortic valve; crosslinking collagen-based material for  
     bioprosthetic devices manufature)  
 IT Collagens, biological studies  
     RL: DEV (Device component use); SPN (Synthetic preparation); THU  
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
     (Uses)  
     (crosslinked; crosslinking collagen-based material  
     for bioprosthetic devices manufature)  
 IT Biocompatibility  
 Calcification  
 Crosslinking  
 Transplant and Transplantation  
     (crosslinking collagen-based material for bioprosthetic  
     devices manufature)  
 IT Aldehydes, reactions  
 Azides  
 Ketones, reactions  
 RL: NUU (Other use, unclassified); RCT (Reactant); RACT (Reactant or  
 reagent); USES (Uses)  
     (crosslinking collagen-based material for bioprosthetic  
     devices manufature)  
 IT Collagens, biological studies  
     RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT  
     (Reactant or reagent); USES (Uses)  
     (crosslinking collagen-based material for bioprosthetic  
     devices manufature)  
 IT 7732-18-5, Water, processes  
     RL: PEP (Physical, engineering or chemical process); PROC (Process)  
     (absorption; crosslinking collagen-based material for  
     bioprosthetic devices manufature)  
 IT 1122-58-3, 4-Dimethylaminopyridine 2592-95-2, N-Hydroxybenzotriazole  
 6066-82-6, N-Hydroxysuccinimide 39743-84-5

RL: NUU (Other use, unclassified); USES (Uses)  
 (crosslinking collagen-based material for bioprosthetic devices manufacture)

IT 66-25-1, Hexanal 111-30-8, Glutaraldehyde 123-38-6, Propanal, reactions 123-72-8, Butanal 420-04-2, Cyanamide 530-62-1, 1,1'-Carbonyldiimidazole 538-75-0, N,N'-Dicyclohexylcarbodiimide 616-02-4, Citraconic anhydride 693-13-0, N,N'-Diisopropylcarbodiimide 830-03-5, p-Nitrophenyl acetate 1865-01-6, p-Nitrophenyl formate 2466-76-4, 1-Acetylimidazole 2491-17-0 2635-84-9, p-Nitrophenyl butyrate 6066-82-6D, N-Hydroxysuccinimide, esters 9046-10-0, Jeffamine D 230 14464-29-0, N-Hydroxysuccinimidyl acetate 16357-59-8, 2-Ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline 25952-53-8, 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride 30364-55-7 74124-79-1, N,N'-Disuccinimidyl carbonate 94820-31-2 152305-87-8

RL: NUU (Other use, unclassified); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)  
 (crosslinking collagen-based material for bioprosthetic devices manufacture)

IT 74-94-2, Dimethylamine borane 75-22-9, Trimethylamine borane 4856-95-5 16940-66-2, Sodium borohydride 25895-60-7, Sodium cyanoborohydride 65605-36-9

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (crosslinking collagen-based material for bioprosthetic devices manufacture)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 1999:7871 HCAPLUS  
 DOCUMENT NUMBER: 130:57274  
 TITLE: Bone graft composites and spacers  
 INVENTOR(S): McKay, William F.  
 PATENT ASSIGNEE(S): SDGI Holdings, Inc., USA  
 SOURCE: PCT Int. Appl., 56 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9856433	A1	19981217	WO 1998-US11611	19980611
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9878185	A1	19981230	AU 1998-78185	19980611
AU 738218	B2	20010913		
EP 988070	A1	20000329	EP 1998-926323	19980611
EP 988070	B1	20040915		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002503992	T2	20020205	JP 1999-502905	19980611
US 6261586	B1	20010717	US 1999-386560	19990831
PRIORITY APPLN. INFO.:			US 1997-873276	A 19970611

WO 1998-US11611 W 19980611

- AB A bone graft substitute including a composition of natural selectively deactivated **bone** material which has been processed to remove associated non-collagenous **bone** proteins, said **bone** material containing native **collagen** materials and naturally associated **bone** minerals and substantially free from native non-collagenous protein, and a therapeutically effective amount to stimulate **bone** growth of a **bone** growth factor in synergistic combination with said **bone** material. Spacers composed of the **bone** graft substitute composition and methods for using the spacers are also provided. A diaphysial cortical **bone** dowel was prepared as well as deactivated allograft and its composite with BMP-2 composite.
- IC ICM A61L027-00
- CC 63-7 (Pharmaceuticals)
- ST **bone** graft composite spacer
- IT **Bone** morphogenetic proteins  
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(2; **bone** graft composites and spacers)
- IT **Bone**  
(artificial; **bone** graft composites and spacers)
- IT **Collagens**, biological studies  
Proteins, general, biological studies  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)  
(**bone** graft composites and spacers)
- IT Growth factors, animal  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)  
(**bone**-derived; **bone** graft composites and spacers)
- IT Transplant and Transplantation  
Transplant and Transplantation  
(**bone**; **bone** graft composites and spacers)
- IT Prosthetic materials and Prosthetics  
(composites, implants; **bone** graft composites and spacers)
- IT **Bone**  
**Bone**  
(transplant; **bone** graft composites and spacers)
- IT 1306-06-5, Hydroxyapatite 7758-87-4, Tricalcium phosphate  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(**bone** graft composites and spacers)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT